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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,180	02/26/2004	Catherine C. Turkel	17679 (BOT)	9912

7590
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08/05/2009

EXAMINER

FORD, VANESSA L

ART UNIT

PAPER NUMBER

1645

MAIL DATE

DELIVERY MODE

08/05/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/789,180

Applicant(s)

TURKEL ET AL.

Examiner

VANESSA L. FORD

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2009.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 and 29 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-20 and 29 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 29 June 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/5508)
Paper No(s)/Mail Date 4/10/09
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

FINAL ACTION

1. This action is responsive to Applicant's amendment and remarks filed February 19, 2009. Claims 1, 9 and 16 have been amended. Claims 21-28 have been canceled. Claims 1-20 and 29 are under examination.

Rejections Withdrawn

2. In view of Applicant's amendment and response the following rejections are withdrawn:
- (a) rejection of claims 1, 9-10, 13-19 and 29 under 35 U.S.C. 101 provisional double patenting, pages 2-4, paragraph 2.
 - (b) rejection of claims 1-3, 10-17, 19-20 and 29 under 35 U.S.C. 102(a), pages 5-6, paragraph 3.
 - (c) rejection of claims 1-20 and 29 under 35 U.S.C. 102(b), pages 6-8, paragraph 4.
 - (d) rejection of claims 1-20 and 29 under 35 U.S.C. 102(b), pages 8-10, paragraph 5.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-3, 10-17, 19-20 and 29 are rejected under 35 U.S.C. 103(a) as unpatentable over Schim (*Current Medical Research and Opinion*, Vol. 20, No.1, January 2001, p. 49-53) in view of Johnson et al (*U.S. Patent No. 5,512, 547 issued April 30, 1996*).

The claims are directed to a method of treating an acute pain medication overuse disorder caused by overuse of acute pain medication, the method comprising the step of local administration of a pure botulinum toxin, wherein the pure botulinum toxin has a molecular weight of about 150 kDa, to a patient with acute pain medication thereby treating the acute pain medication overuse disorder caused by overuse of acute pain medication.

Schim teaches a method of treating medication overuse disorder by administering to a patient botulinum toxin (includes complexing proteins) (page 51). Schim teaches this method because Schim teaches that botulinum toxin was administered to patients with and without analgesic overuse (Study 3, page 51). Schim teaches that botulinum toxin was effective in treating patients with medication overuse disorder (page 51).

Schim do not teach pure botulinum toxin.

Johnson et al teach that pure botulinum toxin (without complexing proteins) has advantages over the botulinum toxin complex because of their high percentage recovery of biologically active neurotoxin and their long-term stability (shelf-life) at temperatures of 0°C which in contrast to the current commercial available products that

have a low percentage recovery of biological active neurotoxin and must be stored at temperatures of -10°C or less (column 4).

It would be prima facie obvious at the time the invention was made to substitute the botulinum toxin complex as taught by Schim for the pure botulinum toxin as taught by Johnson et al used in a method of treating medication overuse disorder because Johnson et al teach that high specific activity preparations reduce the probability of patients developing neutralizing antibodies and it obviously would be desirable to have higher specific activity preparations than those currently available (column 2). Johnson et al teach that the primary advantageous of the compositions of the invention are their high percentage recovery of biologically active neurotoxin and their long-term stability (shelf-life) at temperatures of 0°C which in contrast to the current commercial available products that have a low percentage recovery of biological active neurotoxin and must be stored at temperatures of -10°C or less (column 4). It would be expected, absent evidence to the contrary that administering a composition comprising pure botulinum toxin would be effective in treating medication disorder as well as requiring a lower dosage of botulinum toxin and minimize the development of neutralizing antibodies in these patients.

The Examiner addresses Applicant's comments regarding the primary reference used in the new grounds of rejection set forth above.

Applicant's Arguments

Applicant urges that Schim does not address the needs of patients that take medication in anticipation of rather than in response to a headache, let alone the administration of a pure botulinum toxin in particular, having a molecular weight of about 150 kDa as presently claimed.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed February 19, 2009 have been fully considered but they are not persuasive. It is known in the art that medication overuse patients ingest at least triptan (acute pain medication) drugs at least ten days per month and at least twice a week. See *Cephalalgia, An International Journal of Headache*, Volume 24, Supplement 1, 2004 (*Cephalalgia, 2004*), which teaches that the most common migraine-like headache occurs on ≥ 15 days per month and occur as a mixture of migraine-like and tension-like headaches (page 94). *Cephalalgia, 2004* teach that these patients overuse migraine drugs and/or analgesics (page 94). *Cephalalgia, 2004* teach that diagnostic criterion used for these patients is ≥ 10 days per month of drug use, this translates into 2-3 treatment days a week (page 94). See also *Cephalalgia, 2004, page 95*. Based on the teaching of *Cephalalgia, 2004*, a patient that has a diagnostic criterion of ≥ 10 days per month and 2-3 treatment days is

considered a "medication-overuse headache patient". Thus, by its definition medication-overuse headache patients take acute pain medication in anticipation as well as in response to a headache.

To address the newly added claim limitations, it should be noted that the rejection under 35 U.S.C. 102 has been withdrawn and a new rejection under 35 U.S.C. 103 has been added to address the newly submitted claim limitations.

4. Claims 1-20 and 29 are rejected under 35 U.S.C. 103(a) as unpatentable over in view of *Tepper et al (Cephalagia, 2003, 23, 581-762)* in view of *Johnson et al (U.S. Patent No. 5,512, 547 issued April 30, 1996)*.

The claims are directed to a method of treating an acute pain medication overuse disorder caused by overuse of acute pain medication, the method comprising the step of local administration of a pure botulinum toxin, wherein the pure botulinum toxin has a molecular weight of about 150 kDa, to a patient with acute pain medication thereby treating the acute pain medication overuse disorder caused by overuse of acute pain medication.

Tepper et al teach a method of treating medication overuse disorder by administering to a patient botulinum toxin (includes complexing proteins) (page 715). Tepper et al teach that the patients were administered 100 units of botulinum toxin A (page 715). Tepper et al teach that botulinum toxin was effective in treating patients with medication overuse disorder (page 715).

Tepper et al do not teach pure botulinum toxin.

Johnson et al teach that pure botulinum toxin (without complexing proteins) has advantages over the botulinum toxin complex because of their high percentage recovery of biologically active neurotoxin and their long-term stability (shelf-life) at temperatures of 0°C which in contrast to the current commercial available products that have a low percentage recovery of biological active neurotoxin and must be stored at temperatures of -10°C or less (column 4).

It would be prima facie obvious at the time the invention was made to substitute the botulinum toxin complex as taught by Tepper et al for the pure botulinum toxin as taught by Johnson et al used in a method of treating medication overuse disorder because Johnson et al teach that high specific activity preparations reduce the probability of patients developing neutralizing antibodies and it obviously would be desirable to have higher specific activity preparations than those currently available (column 2). Johnson et al teach that the primary advantageous of the compositions of the invention are their high percentage recovery of biologically active neurotoxin and their long-term stability (shelf-life) at temperatures of 0°C which in contrast to the current commercial available products that have a low percentage recovery of biological active neurotoxin and must be stored at temperatures of -10°C or less (column 4). It would be expected, absent evidence to the contrary that administering a composition comprising pure botulinum toxin would be effective in treating medication disorder as well as requiring a lower dosage of botulinum toxin and minimize the development of neutralizing antibodies in these patients.

The Examiner addresses Applicant's comments regarding the primary reference used in the new grounds of rejection set forth above.

Applicant's Arguments

Applicant urges the pre-emptive use of medication is not associated with an actual pain or ache. Applicant urges that Tepper et al do not even hint at the efficacy of botulinum toxin for treating the pre-emptive use of pain medication, let alone specifies that the botulinum toxin administered is a pure botulinum toxin in particular having a molecular weight of about 150 kDa. Applicant urges that reading Tepper et al the skilled artisan may be lead to believe that medication overuse leads to reductions in headache frequency since Tepper's figure shows there is lower occurrence of headache in medication overusers than in non-overusers at baseline. Applicant urges that Tepper et al do not teach each and every element of the current claims and cannot anticipate the invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed February 19, 2009 have been fully considered but they are not persuasive.

Tepper et al teach that botulinum toxin A is effective in both medication overuse patients as well as patients that are non-overusers. The skill artisan would conclude from the review of Tepper et al that botulinum toxin is effective at treating the two disclosed populations of patients, medication overusers and non- medication overusers.

It is known in the art that medication overuse patients ingest at least triptan (acute pain medication) drugs at least ten days per month and at least twice a week. See *Cephalalgia, An International Journal of Headache*, Volume 24, Supplement 1, 2004 (*Cephalalgia*, 2004), which teaches that the most common migraine-like headache occurs on ≥ 15 days per month and occur as a mixture of migraine-like and tension-like headaches (page 94). *Cephalalgia*, 2004 teach that these patients overuse migraine drugs and /or analgesics (page 94). *Cephalalgia*, 2004 teach that diagnostic criterion used for these patients is ≥ 10 days per month of drug use, this translates into 2-3 treatment days a week (page 94). See also *Cephalalgia*, 2004, page 95. Based on the teaching of *Cephalalgia*, 2004, a patient that has a diagnostic criterion of ≥ 10 days per month and 2-3 treatment days is considered a "medication-overuse headache patient". Thus, by its definition medication-overuse headache patients take acute pain medication in anticipation as well as in response to a headache. Thus, Tepper et al teach the efficacy of botulinum toxin for treating the pre-emptive use of pain medication.

To address the newly added claim limitations, it should be noted that the rejection under 35 U.S.C. 102 has been withdrawn and a new rejection under 35 U.S.C. 103 has been added to address the newly submitted claim limitations.

Status of Claims

5. No claims allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANESSA L. FORD whose telephone number is (571)272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0756. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/
Examiner, Art Unit 1645
August 2, 2009